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Case Report

Serum eosinophil cationic protein levels can be useful for predicting acute exacerbation of asthma

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Abstract

We report on a case in which five consecutive exacerbations of asthma were monitored by following serum eosinophil cationic protein (ECP) levels. The serum ECP level correlated well with each exacerbation and tended to increase even before the exacerbations of asthma became apparent. This case shows that serum levels of ECP can be useful markers of disease activity and may also be predictive markers for acute exacerbation.

Key words: asthma attack, eosinophil cationic protein, predictive marker.

Introduction

One of the important causes of bronchial asthma (BA) is airway inflammation, characterized by the infiltration of eosinophils.[1] Increased levels of eosinophil proteins, such as eosinophil cationic protein (ECP) and eosinophil protein X (EPX) in bronchoalveolar lavage fluid (BALF) and serum in asthmatic patients have also been reported.[2] Other data show that serum ECP levels, in contrast with the total eosinophil count, are correlated with the fluctuation of pulmonary function related to exacerbation.[3,4] Thus, eosinophil proteins in serum or BALF reflect the activation of eosinophils more accurately than the eosinophil count itself. We have measured the serum ECP level, eosinophil count, peak expiratory flow rate (PEF) and pulmonary function in several asthmatic patients. In the present paper we report on a case in which five consecutive exacerbations were monitored over a period of more than 1 year and in whom the serum ECP level correlated well with asthma exacerbation and tended to increase before the appearance of clinical symptoms.

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Case report

A 62-year-old woman with non-atopic asthma presented with symptoms for the first time in 1975. Since 1989, her symptoms worsened and steroid therapy (inhalation and oral administration) was commenced. Serum total IgE was 41.8 U/mL. Skin scratch tests against common inhalants, such as house dust mite and fungi were negative. No other allergic diseases were seen. The factors triggering asthma exacerbation in this case were climate changes, exercise, physical stress, upper respiratory tract infections (URTI) and exposure to dust. Since 1989, the patient has been treated with a standard regimen consisting of the regular use of inhaled beclomethasone and oral theophylline in addition to the use of an inhaled β-adrenoceptor agonist on demand and short-term oral steroids.

The clinical course is shown in Fig. 1. We used the attack score defined by the Japanese Society of Allergology to evaluate the patient's asthma symptoms. Symptoms are divided into five grades (from cough to severe exacerbation), each of which is given a score from 0.5 to 9. The daily attack score was indicated by the sum of four scores recorded by the patient. Five consecutive exacerbations were followed by serum ECP, eosinophil counts and PEF. Blood was collected by venipuncture using an SST tube (Becton Dickinson, Tokyo, Japan) and was allowed to clot at room temperature for 60–120 min. After centrifugation at 1350 *g* for 10 min, serum samples were collected and stored at –20°C. Serum ECP levels were measured every 6 months by a radioimmunoassay

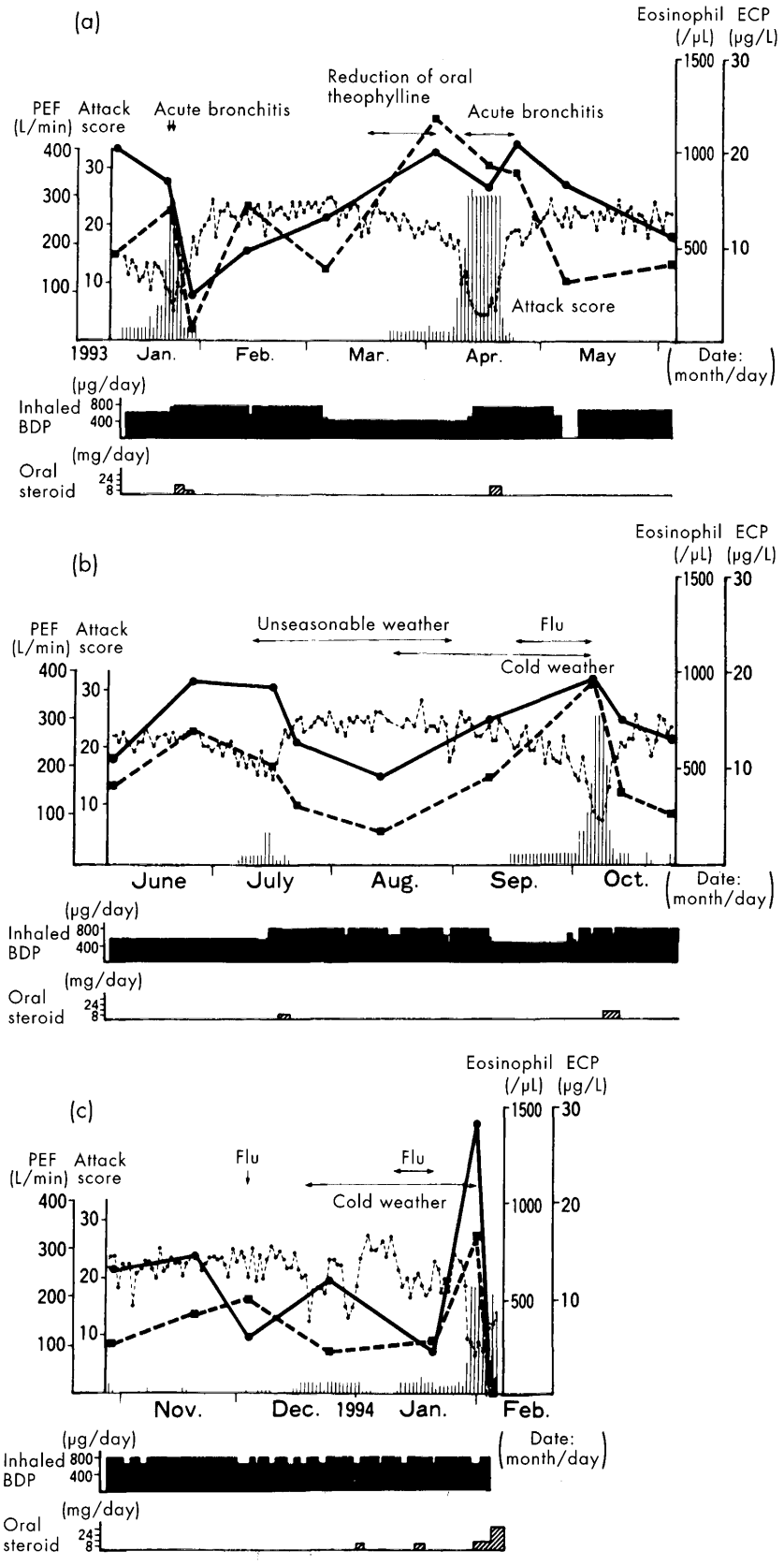

Fig. 1 The clinical course of the patient, showing the change in serum eosinophil cationic protein (ECP) levels (●—●), peripheral eosinophil counts (■--■) and peak expiratory flow (PEF) rates (●--●). Five consecutive exacerbations were followed by well correlated fluctuations of serum ECP levels that tended to elevate even earlier than the appearance of clinical symptoms. (a), (b) and (c) represent consecutive time courses.

(RIA)[5] kit (Pharmacia Upjohn, Tokyo, Japan). Serum ECP levels correlated well with each exacerbation of the asthma and even tended to increase before the exacerbations became apparent, except for the last instance, in which oral steroid administration had commenced before serum sampling. At the times when ECP levels were elevated before exacerbations, the patient did not present with any symptoms or only had a very mild cough. When serum ECP levels were high, the triggering factors, such as URTI and the inhalation of cold air, induced a burst of asthma exacerbation. In contrast, these factors did not precipitate exacerbations when the serum ECP levels were low, such as during August, even if the weather was unstable, and at the beginning of December during a period of URTI. Eosinophil counts were closely related to serum ECP levels, but were dissociated in January 1993, just before the first in a series of attacks, and in December when the patient contracted influenza. The ECP levels seemed to reflect the clinical course more accurately than eosinophil counts. All exacerbations of asthma were well resolved by short-term oral steroid therapy.

Discussion

The present case demonstrated a close relationship between serum ECP levels and asthma activity, whereas the eosinophil counts did not always reflect the clinical course of the asthma. In our experience with other asthmatic patients, both serum ECP levels and blood eosinophil counts were higher in asthmatics compared with levels in patients with either pulmonary emphysema or chronic bronchitis and the serum ECP levels in asthmatics decreased after therapy, whereas the blood eosinophil counts did not.[6] Several methods, including measurement of PEF, pulmonary function tests, biopsy and bronchoalveolar lavage (BAL) are considered useful for monitoring asthma status. Pulmonary function tests and PEF provide information regarding airway function, but do not directly reflect the inflammatory process and may be blunted after the use of bronchodilators. Biopsy of the bronchial epithelium or BAL can demonstrate inflammation, but these procedures are invasive and cannot be used routinely. The total eosinophil count is a measure of both inactive and activated cells. However, ECP is released from activated eosinophils and it has been shown that the serum ECP level is significantly correlated to the level found in BAL fluid.[7,8] Therefore, serum ECP is superior to an eosinophil count of the peripheral blood as an indicator of disease activity and response to therapy and is a more objective parameter of eosinophilic inflammation of the lung.

It has been reported that asymptomatic asthma patients are at risk of developing exercise-induced asthma if their serum ECP levels are increased.[9] In a study on childhood asthma, it was found that serum ECP levels were higher in asymptomatic patients who developed asthmatic symptoms after serum sampling than in those who remained stable.[10] In the present case, serum ECP levels tended to increase before the clinical symptoms became apparent and the precipitating factors did not cause exacerbation when the serum ECP levels were low. These facts suggest that an elevated ECP level could indicate a subclinical active stage that is easily converted to acute exacerbation. Therefore, in selected cases, serum ECP levels can reflect sub-clinically ongoing eosinophilic inflammation of the lung and may be a practical tool for decision making in modifying therapy when asymptomatic asthma patients are encountered.

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